ATL-139

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Michalakis Averkiou et al.
Art Unit: 3305
Serial No.: 08/723,483
Examiner: F. Jaworski
Filed : September 27, 1996

For : ULTRASONIC DIAGNOSTIC IMAGING WITH CONTRAST AGENTS

DECLARATION OF PRIOR INVENTION UNDER 37 CFR §1.131

I, Jeffry E. Powers, an inventor in the above-captioned patent application, declare as follows.

I am an engineer at ATL Ultrasound, Inc., the assignee of the instant patent application. In 1992 I had the responsibility at ATL for coordinating and supporting research with ultrasonic contrast agents by independent research collaborators with ATL. At that time I was collaborating with Peter N. Burns, Ph.D., an ultrasound scientist at the Sunnybrook Health Science Centre in Toronto, Ontario, Canada. Dr. Burns was conducting research into ultrasonic imaging with a harmonic contrast agent identified as SHU 508. In support of this research I provided Dr. Burns with an Ultramark 9 HDI ultrasonic imaging system which had been specially prepared under my direction for his harmonic contrast experiments. Dr. Burns used this UM9 HDI ultrasound system to image with this harmonic contrast agent and obtained a series of harmonic contrast images on January 19, 1992 which are described and shown in the attached report of 28 January 1992 (Exhibit A).

As documented in this report, Dr. Burns used the system's L10-5 transducer probe to transmit ultrasonic pulses at a frequency of approximately 3.2 Mhz. The transducer received a harmonic echo response to this transmission at a frequency of about 6.4 Mhz. These harmonic signals were received by the UM9 HDI system, which filtered the received signals with a programmable digital filter set to its minimum value passband which excluded the 3.2 Mhz transmit frequency and passed the 6.4 Mhz harmonic frequency signals. Attached Exhibit B is engineering documentation of this programmable digital FIR filter which is called a quadrature bandpass (QBP) filter.

The harmonic signals were detected by amplitude detection in the UM9 HDI system, then processed to produce the harmonic

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images shown in Fig. 7-13 which were printed for Dr. Burns' report in addition to being displayed on the system monitor.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Jeffry E. Powers

Date: 7/16/98

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Exhibit A

Harmonic Imaging of Gas-filled Contrast agents with the HDI system

Report of initial experiments, 28 January 1992

In these experiments, the SHU 508 was diluted to about 1/1000th of its in vivo concentration. The HDI transmit waveform was modified as shown. The receive filter bandwidth was reduced to its minimum value and the decimation set to 5 or 6 to create the various narrowband receive images.

The power setting were kept sufficiently low that the contrast agent was within the peak pressure levels that allowed stable harmonic oscillation (less than about 1 atmosphere). Power levels and receive waveforms were measured using a calibrated pvdf membrane hydophone.

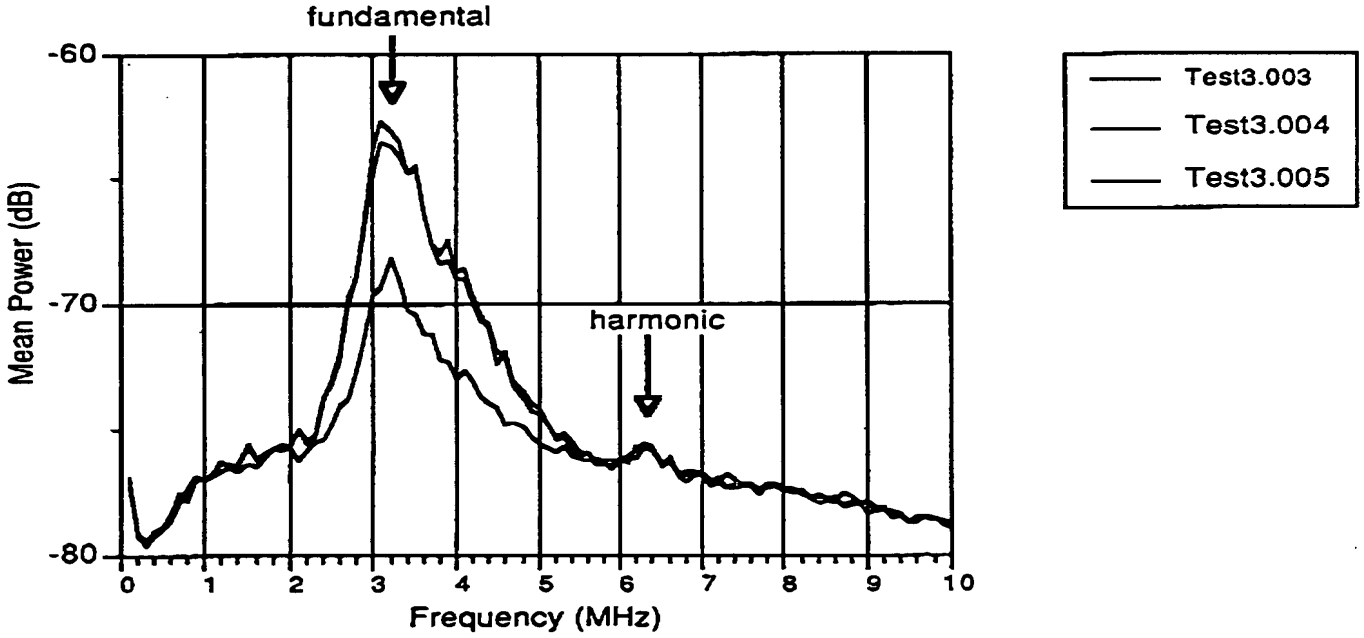

Fig 1. Average power spectra of backscattered echo from contrast agent obtained with hydrophone following broadband burst from transducer with nominal center frequency of 3.5MHz

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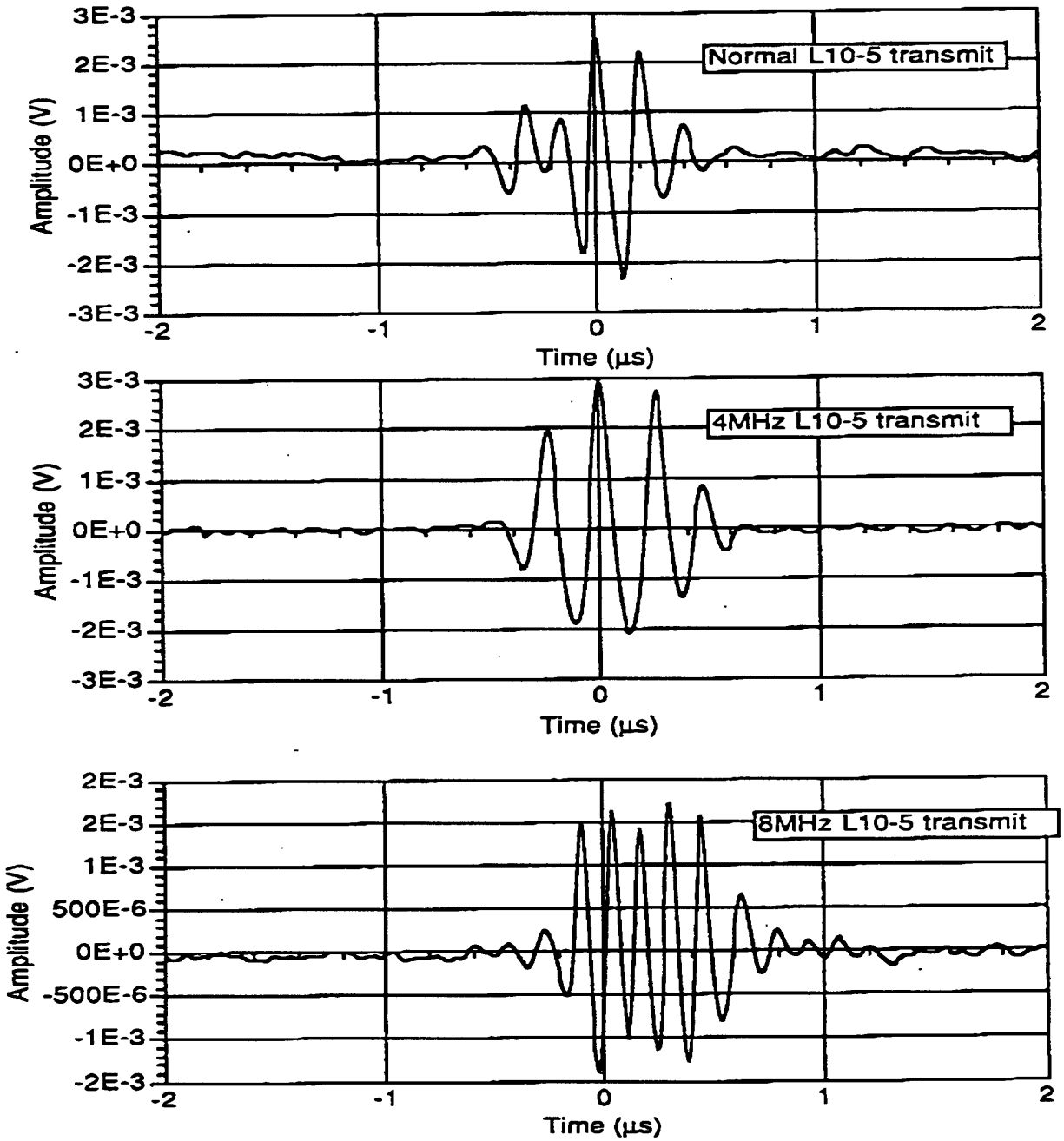

Fig 2. Modified transmit waveforms from UM9 system

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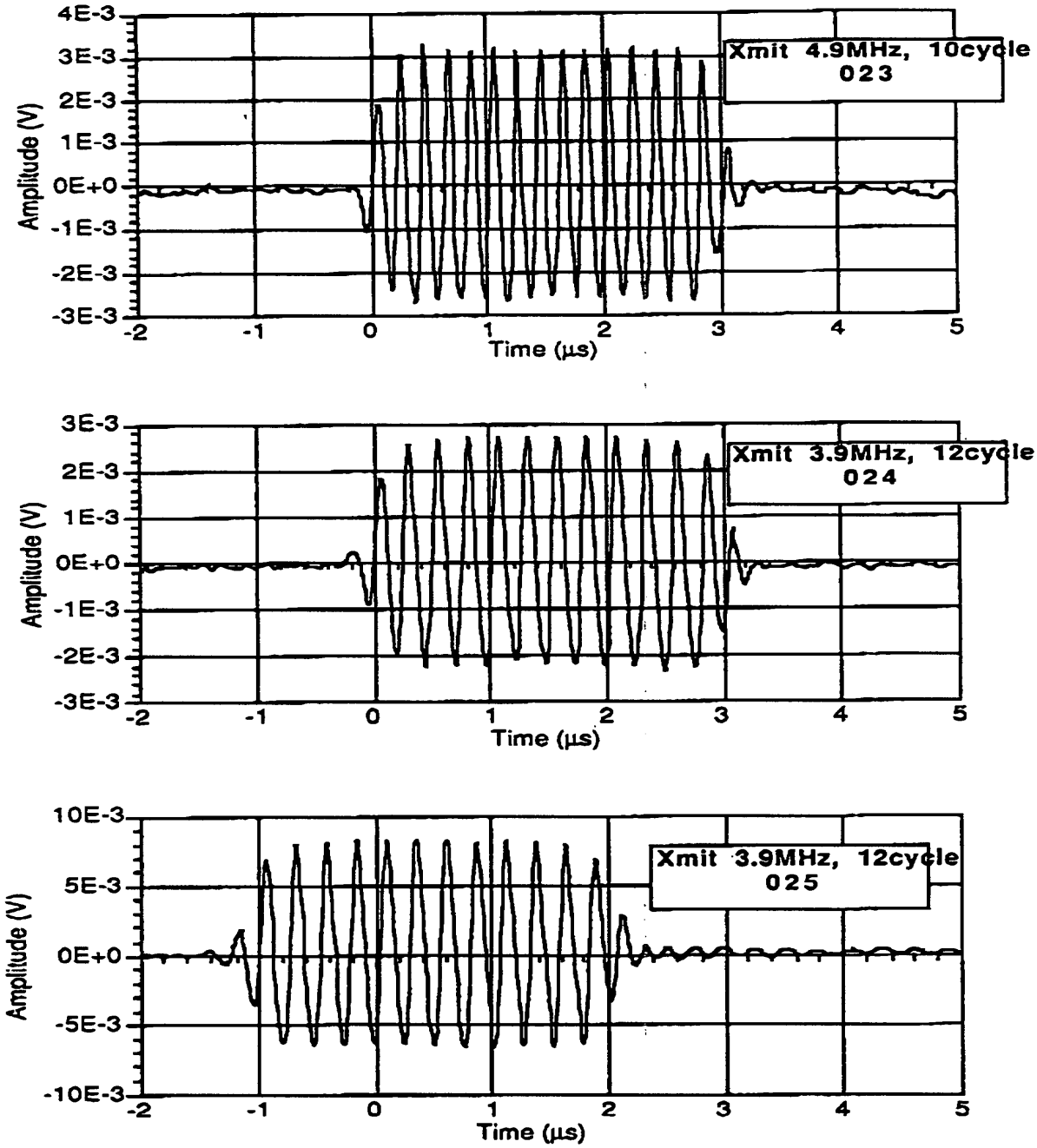

Fig 3. HDI transmit spectra used to obtain harmonic images

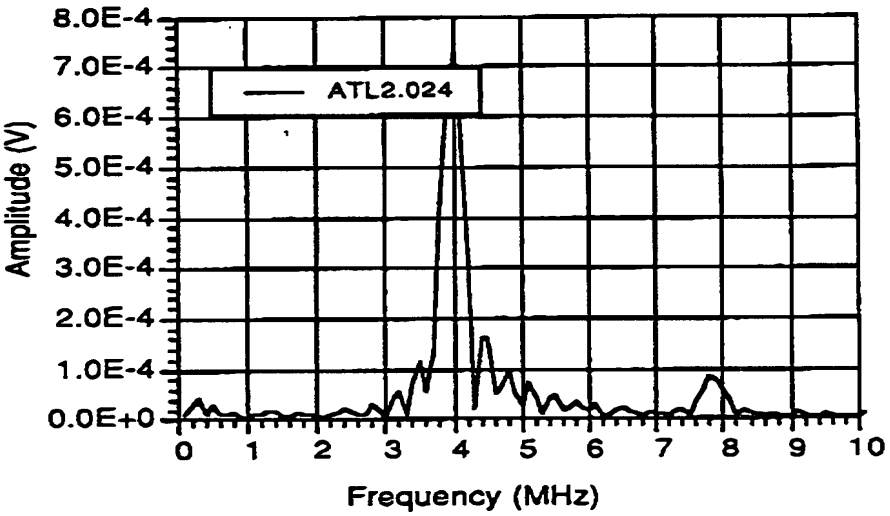

Fig 4. Backscattered m-mode spectrum showing second harmonic

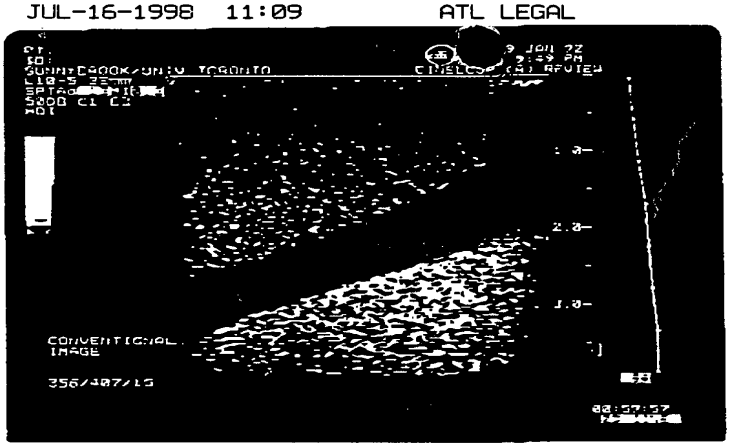

Fig 5. A biogel and graphite test object, with attenuation Of about 0.7dB/cm/MHz. The finger shaped defect in the object is filled with the water. Conventional L10-5 image

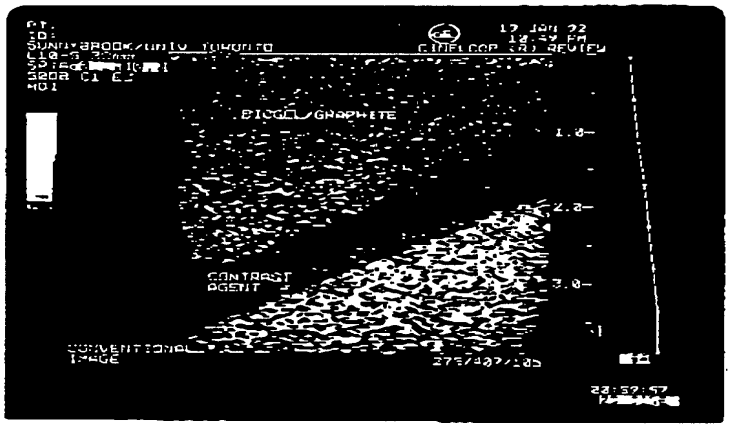

Fig 6. As above, with the contrast agent in the finger. Note echoes.

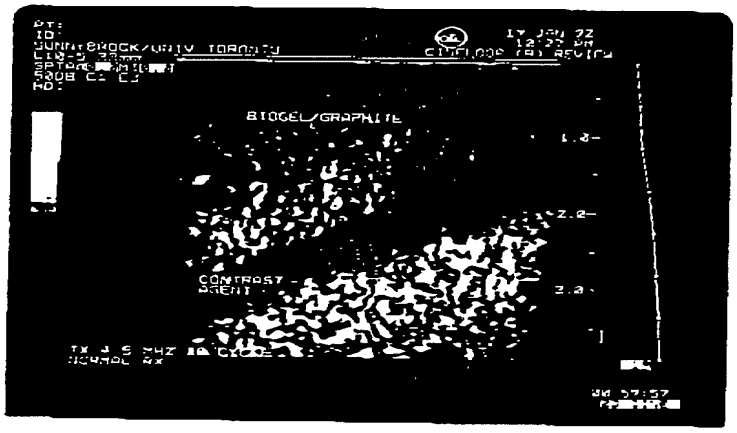

Fig 7. Same object, but imaged with transmit center frequency of 4.5MHz, 10 cycle burst, and normal receive.

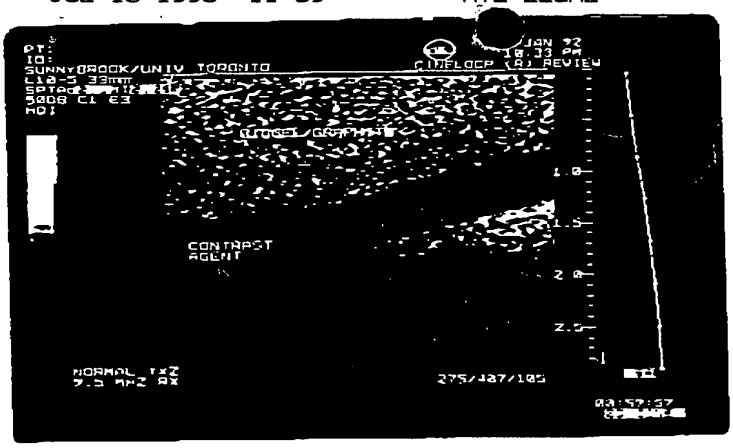

Fig 8. Same object. Normal transmit but 9.5 MHz center frequency receive. Note noise and reduced penetration. Note also reduced echo level of agent .

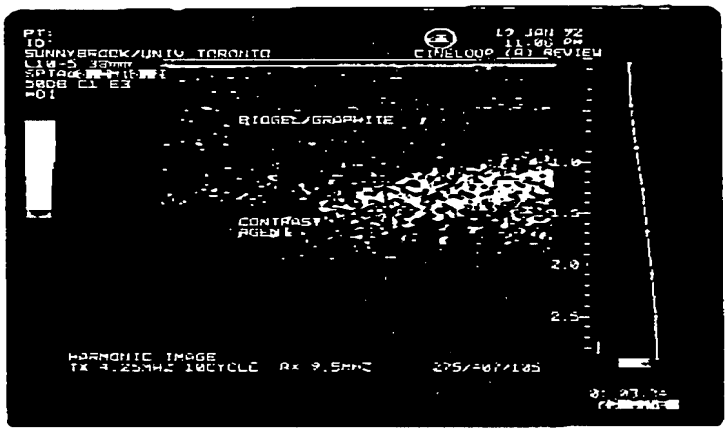

Fig 9. Same object, harmonic image. Transmit 4.5MHz 10cycle, receive 9.1 MHz, narrow band. Note high level of echo from agent. The speckle pattern is now different between agent and test object gel.

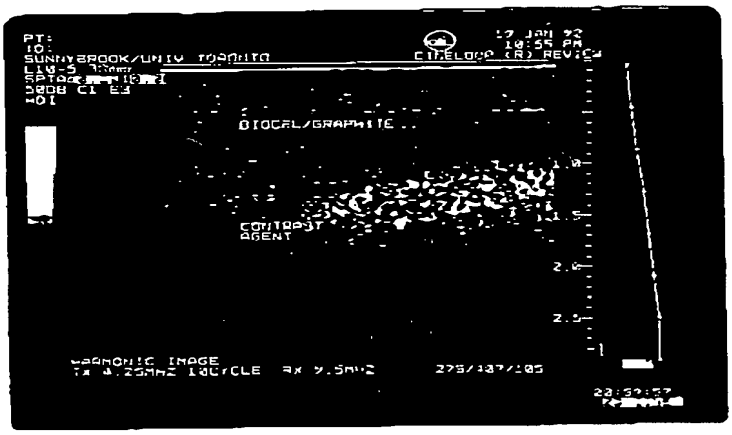

Fig 10. Same object, another harmonic image.

P N Burns, 28 January 1992

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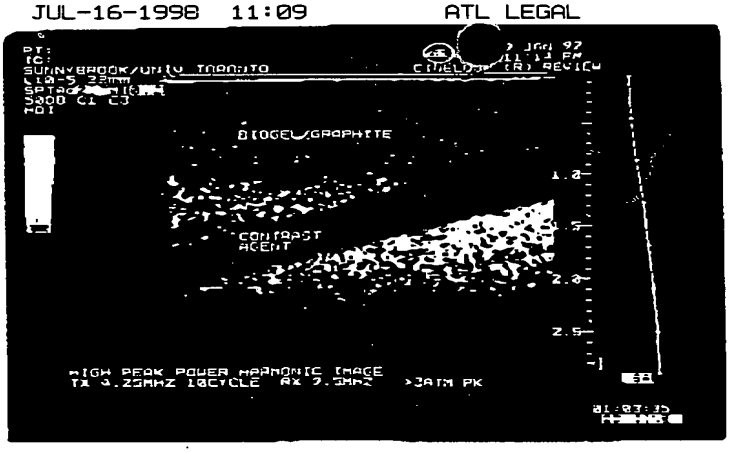

Fig 12. Control harmonic image 1. Same as figs 9&10, but the ultrasound power is increased so that peak pressure is above 3 atmospheres. The agent leaves the stable oscillation regime. Note that the echoes disappear and there is through transmission.

Fig 13. Control harmonic image 2. The contrast agent is replaced with water. Note that the echoes disappear and there is through transmission.

P N Burns, 28 January 1992

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